DETAILED ACTION

Applicant's amendment filed on 2/11/2010 was entered.

Amended claims 1-3 and new claim 5 are pending in the present application.

Response to Amendment

The rejection under 35 U.S.C. 112, first paragraph, for New Matter was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(b) as being anticipated by Nakagawa et al. (US 2002/0197605) was withdrawn in light of Applicant's amendment to claim 1 and cancellation of claim 4.

The rejection under 35 U.S.C. 102(e) as being anticipated by Pompejus et al. (US 6,696,561) was withdrawn in light of Applicants' cancellation of claim 4.

The rejection under 35 U.S.C. 102(b) as being anticipated by Palmieri et al (Arch Microbiol. 165:48-54, 1996) as evidenced by Park et al. (US 2008/0026432) was withdrawn in light of Applicant's amendment.

Claim Objections

Claim 3 is objected because the claim recites "A threonine-producing *Corynebacterium* strain prepared by the method as set forth in claim 2", but it is noted that claim 2 is directed to **a method for increasing the yield of threonine produced** by a threonine-producing *Corynebacterium* strain, and not to a method for preparing a threonine-producing *Corynebacterium* strain.

Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This is because a threonine-producing *Corynebacterium* strain having an endogenous threonine importer gene comprising a continuous DNA sequence from the 1,772 base to the 3,025 base among DNA sequences with the SEQ ID No. 1 must be a *Corynebacterium glutamicum* strain as evidenced at least by the teachings of Nakagawa et al. (US 2002/0197605) which disclosed an isolated *Corynebacterium glutamicum* polynucleotide having SEQ ID NO:1 comprising a nucleic acid sequence (nucleotides 3,231,051 to 3,232,304) that is 100% identical to the DNA sequence from the 1,772 base to the 3,025 base of SEQ ID NO:1 of the present invention (see at least Summary of the Invention, paragraph 20 and SEQ ID NO:1).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. ***This is a new ground of rejection necessitated by Applicant's amendment.***

In amended claim 2, there is no nexus between the pre-amble of the claim reciting "**A method for increasing the yield of threonine produced by** a threonine-producing *Corynebacterium* strain" with the single step of inactivating an endogenous threonine importer gene reciting in the body of the claim. There is no step whatsoever for producing threonine, let alone for increasing the yield of threonine. As written, it is also unclear inactivating an endogenous threonine importer gene of what? Accordingly, the metes and bounds of the claim are not clearly determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended claims 2-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palmieri et al (Arch Microbiol. 165:48-54, 1996) in view of Nakagawa et al. (US 2002/0197605), Pompejus et al. (US 6,696,561) and Simic et al (Journal of Bacteriology 183 :5317-5324, 2001 ; IDS). ***This is a new ground of rejection necessitated by Applicant's amendment.***

Palmieri et al teach that transmembrane threonine fluxes (i.e., uptake, diffusion, and carrier-mediated excretion) **all contributing to threonine production** by a recombinant strain of *Corynebacterium glutamicum*, and they identify a threonine-uptake carrier that transports threonine in symport with sodium ions (see at least the abstract). Palmieri et al also disclose that threonine production can only be observed in mutants or reombinant strains in which threonine biosynthesis is released from feed-back regulation (page 48, col. 2, last paragraph); and that threonine-uptake system is active under conditions of threonine production using the threonine producing recombinant strain MH20-22B-DR17 (page 50, col. 1, last paragraph). In characterizing threonine uptake in *C. glutamicum*, Palmieri et al disclose that threonine is taken up electrogenically in cotransport with Na+ and probably only one Na+ is cotransported with each molecule of threonine (see section titled "Threonine uptake in *C. glutamicum*"). Additionally, drastic reduction of threonine uptake was observed after addition of an excess of serine; and uptake is also inhibited up to >80% by N-ethyl-maleimide (NEM) plus $HgCl_2$ (see at least Table 1; page 51, col. 1, first paragraph).

Palmieri et al do not teach a method comprising the step of inactivating an endogenous threonine importer gene comprising a continuous DNA sequence from the

1,772 nd base to the 3,025th base among DNA sequences with the SEQ ID NO.1; and a threonine-producing *Corynebacterium* strain containing the inactivated endogenous threonine importer gene.

However, at the effective filing date of the present application Nakagawa et al already disclosed the genome of *Corynebacterium glutamicum* having SEQ ID NO:1 comprising a nucleic acid sequence (nucleotides 3,231,051 to 3,232,304) that is 100% identical to the DNA sequence from the 1,772 base to the 3,025 base of SEQ ID NO:1 of the present invention (see at least Summary of the Invention, paragraph 20 and SEQ ID NO:1). Additionally, Nakagawa et al also disclosed an isolated polynucleotide having SEQ ID NO:3350 (1251 nucleotides long) encoding for a **proton/glutamate** symporter or excitatory amino acid transporter 2 that is 99.8 % identical with 100% local similarity to the DNA sequence from the 1,772 base to the 3,025 base of SEQ ID NO:1 of the present invention (see Table 1).

Additionally, Pompejus et al also disclosed an isolated nucleic acid sequence of SEQ ID NO:543 (1058 nucleotides in length) encoding a **proton/sodium-glutamate** symport protein from *Corynebacterium glutamicum* that is 99.8% local similarity to nucleotides 1772-2810 of SEQ ID NO:1 of the present invention (see at least the abstract; Table 1 on page 62; RXN00960 on page 324 and 482).

Furthermore, Simic et al already disclosed a method for constructing various insertion and/or deletion mutants of *C. glutamicum* (see at least the section titled "Construction of strains" on page 5318).

It would have been obvious for an ordinary skilled artisan to modify the teachings of Palmieri et al by also inhibiting threonine uptake of a threonine-producing recombinant *Corynebacterium glutamicum* strain via inactivating an encoding region of the proton/sodium-glutamate symport protein gene in *C. glutamicum* using the approach of constructing insertion and/or deletion mutants in light of the teachings of Nakagawa et al, Pompejus et al and Simic et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because the *C. glutamicum* **proton/sodium**-glutamate gene that is taught by both Nakagawa et al and Pompejus et al is also likely to be involved in threonine uptake since Palmieri et al disclose that threonine is taken up electrogenically in cotransport with Na+ and probably only one Na+ is cotransported with each molecule of threonine. Additionally, Palmieri et al teach that transmembrane threonine fluxes (i.e., **uptake**, diffusion, and carrier-mediated excretion) **all contributing to threonine production** by a recombinant strain of *Corynebacterium glutamicum*. Moreover, the approach of constructing insertion and/or deletion mutants of *C. glutamicum* has been successfully demonstrated by Simic et al for various different genes.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Palmieri et al, Nakagawa et al, Pompejus et al. and Simic et al, coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

The modified method and the modified threonine-producing *C. glutamicum* resulting from the combined teachings of Palmieri et al, Nakagawa et al, Pompejus et al.

and Simic et al as set forth above are indistinguishable form those being claimed by the present application.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

Claim 1 is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/QUANG NGUYEN/

Primary Examiner, Art Unit 1633